WELLCOME INSTITUTE LIBRARY
Coll. welTROmec
Call No. pam WC715 1902 R72n

NOTE ON SERUM REACTIONS AND THE TEMPERATURE CURVE IN CHRONIC MALARIA INCLUDING KALA-AZAR

L.Rogers.

Indian Medical Gazette, 1902.

22200060169

Vol. 37.

Original Articles.

NOTE ON SERUM REACTIONS AND THE TEMPERATURE CURVE IN CHRONIC MALARIA INCLUDING *KALA-AZAR*.

By LEONARD ROGERS, M.D., M.R.C.P., CAPTAIN, I.M.S.,

Offg. Professor of Pathology, Medical College, Calcutta.

Before the days of the malarial parasite and serum reactions, no one seems to have doubted the truly malarious nature of the class of cases known under the term "malarial cachexia," a condition occurring in such numbers in very malarious parts of India, Algeria and elsewhere as a direct sequel of repeated attacks of fever indistinguishable clinically from malaria. Recently, owing to the difficulty in finding parasites in this last stage of the disease and the failure of quinine to influence some advanced cases of this cachexial condition, doubt has been thrown in some quarters on their malarial nature. For months past I have been studying this question as part of a comprehensive investigation of all long continued fevers met with in the unrivalled material in the Calcutta hospitals, and hope shortly to be able to find time to work out and formulate my conclusions. In the present communication I only propose to deal with the serum reactions and temperature curves, as this point has been raised in the September issue of this journal. I have carried out a number of serum tests for both typhoid and Malta fevers, in cases of chronic malarial fevers during the last two years with such uniformly negative results that it is unnecessary to enter into details regarding them except to mention that the absolutely reliable microscopic method with a time limit of one hour with living cultures was always used. The bacteriological and blood examinations of these cases I must reserve for a future communication, but I may say that they are similar to those I have previously described in both chronic malaria of districts of Assam, which were free from *kala-azar*, and, in the last named disease, only I have extended my observations in some directions. Dr. Bentley's highly ingenious hypothesis that this last disease is nothing but a severe type of "epidemic Malta fever" introduced into India by troops from the Crimea at present rests solely on the serum tests recorded in his paper in the last issue, a piece of evidence, which, fortunately, it is possible to submit to rigid examination. I would, however, suggest that Dr. Bentley's theory would obtain strong support if he could unearth some records of a similar "epidemic Malta fever" in the neighbourhood of the English hospitals where the infinite majority of troops returning from the Crimea were accommodated. I fear, however, it will puzzle even Dr. Bentley to explain how the Burdwan epidemic fever can have originated from Malta fever introduced by European troops at the time of the Mutiny, as he suggests, considering that the "fever was very fatal in the Jessore district in the years 1847-48," *vide* Bengal Census Report of 1881. Dr. Bentley has omitted to state in his paper that he first sent me the blood of some *kala-azar* cases to test for Malta fever, in none of which was I able to obtain a positive result even in dilutions, of 1 in 10. In sending the bloods he stated they were from fever cases which resembled closely undulant or Malta fever, suppressing the fact that they were *kala-azar* cases, doubtless, so that I might be quite unprejudiced in carrying out the tests. The question, then, resolves itself into one of which series of tests is correct, for purposes of judging which it is necessary to know exactly how each were carried out, a point on which no information is vouchsafed in Dr. Bentley's paper. The very low dilutions with which he records reactions, as compared with those in dilutions of from 1 in 150 to 1 in 1,000 uniformly obtained in the cases of Malta fever on which Professor Wright's and Captain Smith's original communication on the subject (*British Medical Journal*, March 16th, 1897) were based, at once strikes one. Further, no explanation is offered of the negative results in nearly one quarter (6 out of 25) even in the extremely low dilution of 1 in 10, or of the absence of complete reactions in more than half the cases (13 out of 25) in the low dilutions of 1 in 40; although reactions can be obtained from the fifth day up to thirteen months after the onset of Malta fever.

In view of the absence of details of Dr. Bentley's reactions, and the very inconstant and inconclusive nature of the reactions obtained, I have recently repeated my tests on a series of nine more *kala-azar* cases, the bloods of which were kindly sent me by Dr. Dodds Price of the Nowgong district, than whom no living medical man has had such a close and prolonged acquaintance with the disease. As in the case with my former tests on Dr. Bentley's *kala-azar* cases, the indisputably accurate microscopical method with a time limit of one hour was used. As I have been credibly informed that the method commonly adopted at the Kasauli Institute is the use of sedimentation tubes, I also put up a control series in these tubes in the same dilutions as in Dr. Bentley's series. The results were highly instructive, for typical precipitates at the end of 24 hours were obtained in the sedimentation tubes in very similar proportion and degree to those reported from Kasauli. Yet by the microscope test, complete clumping was not obtained in a single case, even in dilu-

tions of 1 in 10, at the end of one hour, although Aldridge states that true Malta fever serums clump the micrococcus melitensis "immediately" in this dilution. Further, the precipitates in the sedimentation tubes were examined microscopically after from 24 to 72 hours, and even then many of the micrococci were found to be still active and not clumped. In one of these bloods red corpuscles were present in some numbers, and in two others a few were found, but in the remaining six cases none were present, which could not account in any way for the precipitates. I noticed, however, that most of the serums were more or less stained with hæmoglobin, this being nearly inevitable with bloods which have been sent several days' journey. I therefore tested some similar bloods from cases of cholera, cerebrospinal fever and dysentery, and got similar precipitates with the Malta fever coccus in low dilutions in sedimentation tubes, although the cocci were still active under the microscope. It is clear, therefore, that in bloods which have travelled for several days the sedimentation tests alone are not reliable, so that apart from the question, whether the inconstant reaction in the low dilutions recorded by Dr. Bentley are any evidence at all of Malta fever, it is clearly necessary to know by what method they were obtained, before any value whatever can be assigned to them, especially in view of my negative results by the accurate microscopical method in two series of *kala-azar* cases from two different districts of Assam, including those sent by Dr. Bentley himself. The only conceivable source of fallacy in my results is the bare possibility of my cultures being wrong, but this can safely be discounted, as in my last series of cases I used two different cultures in each case, one derived from a reliable European source and the other very kindly supplied to me by Major Semple himself from the Kasauli laboratory. It would not be very surprising if Malta fever is found to occur in Assam, as in other parts of India, but the low serum reactions recorded by Dr. Bentley do not conclusively prove even that much.

Since writing the above I have heard from Major Semple that he controls the sedimentation test by microscoping a portion of the mixture for clumping. This narrows the question of the value of Dr. Bentley's reactions down to one of whether reaction in such low dilutions at 1-10 and 1-40 are reliable evidence of Malta fever. The opinions of medical men who have watched cases in which such reactions have been obtained as to whether they presented the clinical picture of Malta fever or not, will be of great value here. My own experience, is that reactions in dilutions of 1 in 10 with Malta fever organism, may occasionally be obtained in cases which present no clinical evidence of Malta fever, and I come to regard such reactions as of no diagnostic value whatever. I should also add that Major Semple only looks on his reactions as evidence that Malta fever does occur in Assam, as in other parts of India, and not as in any way proving that *kala-azar* is Malta fever.

In view of the negative serum reactions recorded above in *kala-azar* it would be a waste of space to criticise in detail Dr. Bentley's arguments. One crucial point may, however, be briefly considered with advantage, namely, the temperature curves in relationship to the death-rates in Malta fever and *kala-azar* respectively. All specific fevers have more or less definite temperature curves and course, so that if these two diseases are one and the same, these should be similar, except in so far that as *kala-azar* is many times as fatal as Malta fever, its course should, in the great majority of cases, resemble the malignant type of Malta fever, only be infinitely more malignant than the latter ever is in Europe. Let us see how far this is the case.

Taking Hughes' detailed account of the Malta fever temperature curve we find that he divides his cases into three classes, namely, the malignant, undulant and intermittent type. The first, which alone is at all commonly fatal, presents a severely remittent type throughout, death occurring in 5 to 21 days in fatal cases. *Kala-azar* being so many times more fatal than Malta fever should usually occur in this form if the two diseases are the same, yet such a type of the disease is absolutely unknown to me either in my years' continual investigation of the affection in Assam or in the literature of the disease. The second or "undulant" type comprise the majority of Hughes' cases, being characterised by a series of waves of remittent fever, averaging ten days in duration and three in number, with very short intervals of little or no fever between them, averaging three to four days and ending abruptly "with a subnormal temperature lasting from one to six or more days with a clean tongue," this being "one of the surest signs of permanent cessation of the pyrexia." Further he states that "*when, however, the patient is completely free from the disease, it does not, like paludism, recur,*" except for mild pyrexia accompanying the common complications of effusion into the joints and swollen testicle, complications which I never once met with in *kala-azar*, although the first-mentioned occurs in no less than 40 per cent. of Malta fever cases, forming one of the most characteristic features of that disease. I have just re-examined a series of my original temperature charts of *kala-azar* cases, with the result that I could not find a single one at all comparable with the malignant type of Malta fever, and only one which at all resembled the common undulant type, these being the two types which may be fatal in the case of Malta fever. Lastly, with regard to the very mild and scarcely ever fatal intermittent type of Malta fever, I have found five charts in which the apyrexial intervals were sufficiently short to allow of their present-

ing some resemblance to the intermittent type of Malta fever, but four of these died, and the other was lost sight of when in a desperate condition. Of the remaining twenty-three cases the intervals between the irregularly recurring intermittent fever were far longer than occurs except very rarely in Malta fever, so that if they were cases of that disease the type of fever was far milder than is seen in Europe in this non-fatal form of the disease. Yet only two of them recovered, the rest proving fatal. *We arrive, then, at the* reductio ad absurdum *that the manifold more fatal* kala-azar *yet presents, as a general rule, a far milder type of fever curve than the mildest non-fatal form of Malta fever.* Again, we have seen that once the temperature has remained normal for some days Malta fever does not recur. On the contrary, the inveterate tendency of *kala-azar*, as of all chronic malarial fevers, is to relapse again and again with frequent and often considerable intervals of apyrexia, sometimes lasting for several months in the cold weather. In my original report I wrote: "Thus there is no definite type of fever in the disease, while its duration, and that of the intervals between the attacks, differ widely, the only constant characteristic being the inveterate tendency to recur again and again until a fatal issue results." The types of the temperature curves of the two diseases then agree only in the single point that both may run a very prolonged course, although even this is as rare in fatal cases of Malta fever as it is common in *kala-azar*, which leads me on to the last point which appears worthy of discussion, namely, the death-rate and the duration of fatal cases. In my report I gave the death-rate of 200 consecutive cases of *kala-azar* on Nowgong tea gardens, which had been diagnosed and treated throughout by no less an experienced practitioner than Dr. Dodds Price, as 96 per cent. This rate was subsequently reduced to a little over 50 per cent., mainly on account of more vigorous and sustained anti-malarial treatment than before, to prevent the retrogression from which beneficial result is the main object of the present communication. Now the death-rate of Malta fever is given by Hughes as about 2 per cent., while 60 per cent. of the fatal cases terminated within one month, and 84·44 per cent. within two months, of the onset of the fever. *Kala-azar* being from 25 to 48 times as fatal as Malta fever, it should show a very much greater proportion of rapidly fatal cases if the two diseases are the same. Yet in my report I recorded the fact that the average duration from the first admission for fever to the date of death taken from 193 cases on a Nowgong tea garden was 7·4 months, the extremes being two months to three years, while the usual duration was from 4 to 9 months. These facts (not to mention many others such as the absence of joint and testicle sequelæ and the darkening of the skin, which is so characteristic a feature as to give the disease its name) taken with the extremely high death-rate and the totally different temperature curves are amply sufficient to prove the two diseases to be entirely distinct. It was, indeed, these essential differences between *kala-azar* and Malta fever, which made me consider it unnecessary to even discuss the possibility of their identity in my comprehensive report on the former affection. If *kala-azar* can be proved to be Malta fever, then the clinical history of the latter will have to be entirely rewritten. In the meantime the negative serum reactions obtained by me with the absolutely reliable microscopical method in two series of cases of *kala-azar*, the marked reduction in the mortality of the disease by steady anti-malarial treatment in the hands of Dr. Dodds Price, and the complete success of the segregation measures that Dr. Price carried out at my suggestion, with the result that his new lines with some 450 coolies have remained entirely free from the disease for five years, justify me in maintaining my original position that *kala-azar* is an epidemic malarial fever, supported as it is by no less an authority on malaria than Major Ronald Ross after an independent investigation in Assam.

NOTE ON *KALA-AZAR*.

By J. DODDS PRICE, M.R.C.S. (Eng.), L.R.C.P. (Lond.),

District Medical Officer, Nowgong, Assam.

My attention has been drawn to an article by Dr. Charles Bentley, which appeared in the September number of this *Gazette*, on some recent discoveries he has made as to the true nature of *kala-azar*.

Having examined and treated nearly 2,000 cases of the disease, and having been brought into almost daily contact with *kala-azar* for nearly nine years, may I be permitted to state my belief that the disease is of malarial origin and to give my reasons for this opinion.

I am anxious to do this, as I feel that a great deal of harm may be done by Dr. Bentley's paper if his theory is accepted out of hand, and the anti-malarial treatment of *kala-azar* dropped without further enquiry.

I must also confess to considerable surprise at one or two statements made by Dr. Bentley, and I cannot help thinking that he has allowed himself to be too easily influenced by the results of Major Semple's blood examinations. While visiting this district in April last, Dr. Bentley certainly found malarial parasites in the blood of every case of *kala-azar* I shewed him, and similar parasites were present in the blood of all the cases of *kala-azar* we examined together in Tezpur a month later. In addition, Dr. Bentley shewed me a number

WELLCOME LIBRARY INSTITUTE